Abstract: P1049

Title: RUXOLITINIB TREATMENT IN PATIENTS WITH POLYCYTHEMIA VERA REDUCES JAK2 ALLELE BURDEN AND IMPROVES HEMATOCRIT CONTROL AND SYMPTOM BURDEN

Abstract Type: Poster Presentation

Topic: Myeloproliferative neoplasms - Clinical

Background:

In the pivotal RESPONSE and RESPONSE 2 trials, the Janus kinase (JAK)1/JAK2 inhibitor ruxolitinib (RUX) was superior to best available therapy (BAT) at providing hematocrit control, complete hematologic response, and improving disease-related symptoms in patients (pts) with polycythemia vera (PV).

Aims:

To report results of a post hoc pooled efficacy analysis using data from the RESPONSE studies.

Methods:

RESPONSE and RESPONSE 2 were randomized, open-label, multicenter, phase 3 trials that assessed efficacy and safety of RUX in adults with PV who had resistance/intolerance to hydroxyurea. Splenomegaly was required for RESPONSE but not RESPONSE 2; pts in both studies were randomized 1:1 to RUX (starting dose, 10 mg twice daily) or BAT (most commonly hydroxyurea [59%, 49%] or interferon formulations [12%, 13%] in RESPONSE and RESPONSE 2, respectively). Pts randomized to BAT in either trial could cross over to RUX at the time of primary analysis (Wk 32 in RESPONSE; Wk 28 in RESPONSE 2) or later for efficacy or safety reasons. In this pooled analysis, hematocrit control (hematocrit <45% maintained since Wk 16 with ≤1 phlebotomy occurring postrandomization and before Wk 4) was assessed at Wk 28 and 80. Symptom control using the Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS) and changes in *JAK2*V617F allele burden were also assessed. Response rate 95% CIs were calculated using the Clopper-Pearson exact method; odds ratio (OR) and 95% CI for comparisons of proportions of pts achieving ≥50% reduction from baseline in MPN-SAF TSS were calculated by the Mantel-Haenszel method.

Results:

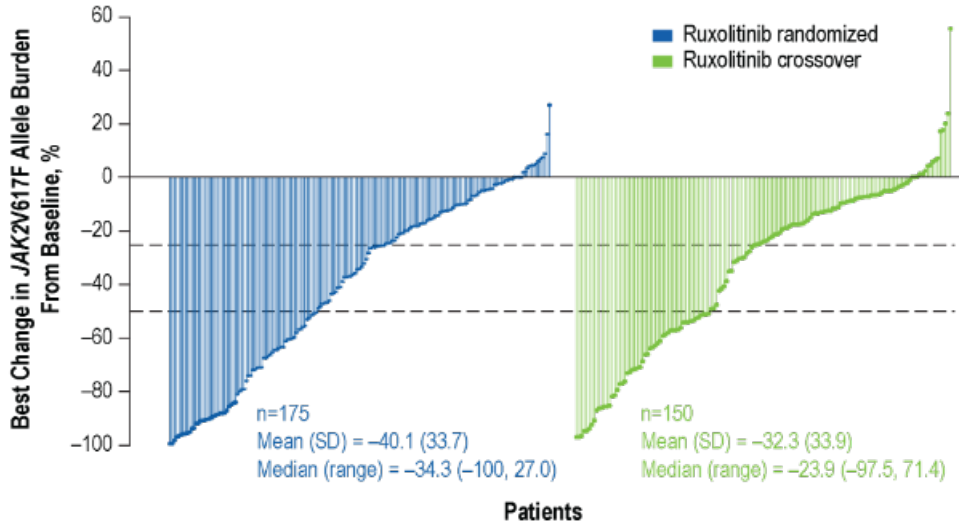
Overall, 371 pts were randomized in RESPONSE and RESPONSE 2 (RUX, n=184; BAT, n=187). Pt baseline characteristics were similar across trials and treatment groups. Median (range) age in the overall pooled analysis population was 62.0 (26–90) years; most pts were male (62.5%) and White (88.1%). At Week 28, 62.0% (95% CI, 54.5%–69.0%) of RUX pts achieved hematocrit control vs 18.2% (12.9%–24.5%) of BAT pts. Durable hematocrit control was maintained to Wk 80 by 47.3% (95% CI, 39.9%–54.8%) of pts randomized to RUX (nearly all BAT pts crossed over to RUX). More pts receiving RUX vs BAT achieved ≥50% reduction from baseline in MPN-SAF TSS at Wk 16 (the only common timepoint in both studies; 48.7% [95% CI, 40.7%–56.8%] vs 18.0% [95% CI, 12.5%–24.6%]; OR, 4.3 [95% CI, 2.6–7.2]). Mean (SD) change from baseline to Wk 16 in MPN-SAF TSS was −4.4 (10.0) for RUX pts and 0.6 (6.9) for BAT pts. *JAK2*V617F allele burden decreased consistently from baseline to Week 208 in RUX patients. Mean *JAK2*V617F allele burden in pts randomized to RUX decreased from 66.1% to 41.4% at 4 years. A ≥25% decrease in *JAK2*V617F allele burden was observed in 57.1% of pts randomized to RUX and ≥50% decrease in 38.9%; similar reductions were observed following crossover from BAT to RUX (**Figure**), with decreases of ≥25% and ≥50% in 48.7% and 35.3% of pts, respectively. Analysis of the BAT group (limited by small pt numbers after Wk 32) showed a best decrease of ≥25% and ≥50% in 7.2% and 2.6% of pts, respectively.

Summary/Conclusion:

In this pooled analysis of RESPONSE and RESPONSE 2, pts with PV treated with RUX achieved durable

hematocrit control through Wk 80 and had better symptom control at Wk 16 than those who received BAT. Reductions in *JAK2*V617F allele burden were consistently observed through Wk 208 in pts treated with RUX, including those who crossed over from BAT. Taken together, these results provide further evidence of the pt benefit of RUX in pts with PV with or without splenomegaly.

Figure: Best Change in *JAK2*V617F Allele Burden From Baseline



Dashed lines indicate −25% and −50% change from baseline.

Keywords: Ruxolitinib, Janus Kinase inhibitor, Polycythemia vera